REMARKS

The above amendments and these remarks are responsive to the Office action dated September 16, 2004. Claims 1-7 are pending in the application. Claims 1-7 are rejected. By way of the present amendment, claims 1, 2, 3 and 7 are amended; claims 4-6 are canceled; and new claims 8-13 have been added. In view of the amendments above, and the remarks below, applicant respectfully requests reconsideration of the application under 37 C.F.R. § 1.111.

Amendments to the Claims

Applicants take this opportunity to amend the pending claims. Claims 4-6 are canceled, without prejudice. Claim 1 is amended to more particularly recite the claimed invention. In addition, the compound MUN-014 has been excluded from the scope of compounds recited in claim 1. Support for the amendment is found in the specific disclosure of compound MUN-014 in the specification (see page 14). The explicit exclusion of MUN-014 from the claims is therefore supported by the disclosure as filed.

New claims 8-13 are added. Support for the new claims is found in claims 1-7 as originally filed, and in the specification generally at page 5, lines 12-37.

Rejections under 35 USC § 112

Claims 1-7 are rejected under 35 U.S.C. § 112, first paragraph. The Examiner has indicated that the specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in

scope with these claims. In particular, the Examiner suggests that the specification fails to enable the inhibition of MCP-1 production with the disclosed glycyrrhizin derivatives wherein R^1 is hydrogen or a group of formula (III) and the derivatives wherein R^2 is a group of formula (IV).

The Examiner suggests that such compounds are substantially different structurally from glycyrrhizin, and therefore there is reason to doubt that additional glycyrrhizin derivatives would have the same activity as glycyrrhizin. Applicant respectfully suggests that the question of whether the specification enables the claimed invention is distinct from Applicant's assertion that the disclosed compounds possess the utility indicated by the specification, and that in any event, the claimed invention is fully enabled by the specification.

The first paragraph of 35 U.S.C. § 112 states that the specification shall include the manner and process of making and using the invention, or the enablement requirement. The Examiner has rejected claims 1-7 because the specification allegedly fails to comply with the enablement requirement. In particular, the Examiner states that the specification does not reasonably provide enablement for inhibiting MCP-1 production with glycyrrhizin derivatives wherein R^1 is hydrogen or a group of formula (III) and the derivatives wherein R^2 is a group of formula (IV). Applicants respectfully disagree.

<u>The Claimed Invention is Enabled</u>

It is established that the subject matter of a claim is enabled where one reasonably skilled in the art could make or use the invention from the disclosures in the specification,

coupled with information known in the art, without undue experimentation. A patent need not teach, and preferably omits, what is well known in the art. The mere fact that experimentation may be required does not result in a lack of enablement. The test of enablement is not whether any experimentation is necessary, but if experimentation is necessary, whether it is undue (see MPEP § 2164.01).

In the instant case, to comply with 35 U.S.C. § 112, first paragraph, the specification must teach an artisan of ordinary skill how to make and administer glycyrrhizin and glycyrrhizin derivatives as recited in the instant claims, without requiring undue experimentation. Applicant suggests that the specification provides sufficient guidance that an artisan of ordinary skill could practice the claimed invention.

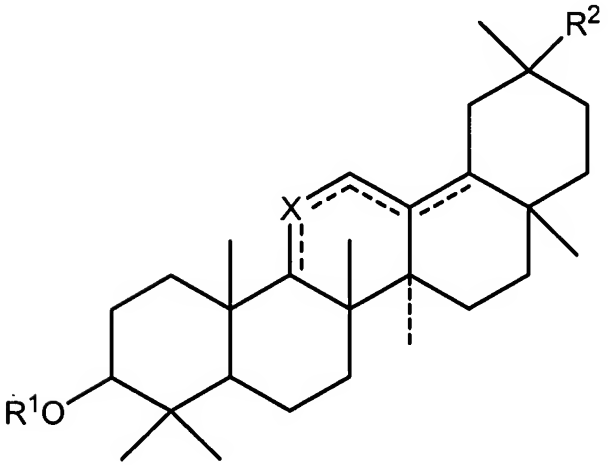
First, the glycyrrhizin derivatives utilized in the claimed invention are either commercially available (see page 6, lines 15-17), or may be prepared according to published methods (see page 6, lines 18-21), or according to general methods described in the specification (see page 6, line 22 to page 8, line 13).

In addition, the specification details the administration of glycyrrhizin and glycyrrhizin derivatives to peripheral blood mononuclear cells (Examples 1-3), and the subcutaneous administration of glycyrrhizin to mice (Example 4). Applicant suggests the teaching of the specification is sufficient for an artisan of ordinary skill, such as a clinician, to obtain and administer the glycyrrhizin compounds as claimed in the rejected claims. One reasonably skill in the art would be well aware of how to prepare and administer medicaments such as the disclosed glycyrrhizin compounds.

<u>The Claimed Invention Possesses a Specific and Substantial Utility</u>

Applicant has asserted that the claimed invention has a specific and substantial utility that would be considered credible by a person of ordinary skill in the art. However, the Examiner has suggested that glycyrrhizin derivatives having significantly different structural formulas encompassed by the instant claims would not exhibit have the same activity as glycyrrhizin, and that the Applicants have not demonstrated the utility of the full scope of the invention with respect to such compounds. Applicant suggests that the full scope of the claimed invention possesses utility under 35 U.S.C. § 101, as demonstrated by the specification as filed.

The glycyrrhizin derivatives of the instant claims share a common core structure having a general formula I:



... (I)

The structure of Formula I has three variables: X, R^1 and R^2.

A variety of glycyrrhizin derivatives are shown in the specification to have specific utility for inhibiting MCP-1 production. In particular, the derivatives GR, MUN-

003, MUN-011, MUN-013, MUN-016, and MUN-018 are each demonstrated to inhibit MCP-1 production in peripheral blood mononuclear cells (PBMC), as recited in Example 1, and shown in Fig. 1. As shown in the specification at page 14, and tabulated below, the glycyrrhizin derivatives of Example 1 include compounds having representative X, R^1, and R^2 substituents:

Compound No.	X	R^1	R^2
GR	CO	Formula II	COOH
MUN-003	CH	Formula II	COOH
MUN-011	CO	H	COONa
MUN-013	CH	Formula III	Formula IV
MUN-016	CH	Formula III	COONa
MUN-018	CO	Formula III	COONa

That is, contrary to the Examiner's assertion, Applicants have indeed shown that a compound having R^1 that is hydrogen is an effective MCP-1 inhibitor (MUN-011), and that compounds wherein R^1 has Formula III are effective MCP-1 inhibitors (MUN-013, MUN-016, MUN-018).

Furthermore, Applicants suggest that as the MCP-1 inhibition demonstrated by glycyrrhizin is shared by the compounds recited in claim 1, as shown in Figure 1 and Example 1, that the ability of glycyrrhizin to inhibit MCP-1 in isolated cells and in mammals (see Examples 2-4) is similarly shared by the compounds recited in claim 1.

Applicants have demonstrated the efficacy of a number of representative examples of the compounds of claim 1, and suggest that they have provided sufficient evidence that the asserted specific and substantial utility would be considered credible by a person of ordinary skill in the art. Applicants have also provided sufficient guidance that one of reasonable skill in the art would be well aware of how to prepare and administer the disclosed glycyrrhizin compounds. Applicants therefore request the withdrawal of the rejection of claims 1-7 under 35 U.S.C. § 112, first paragraph for lack of enablement.

The Examiner has rejected claims 5 and 7 under 35 U.S.C. § 112, first paragraph, because the specification does not reasonably provide enablement for an infection control with any compound as encompassed by claim 5, or for treatment or prevention of decreases in infection resistance as encompassed by claim 7. Applicants respectfully disagree.

As Applicants have canceled claim 5, the rejection of that claim is rendered moot. With respect to claim 7, Applicants suggest that, as discussed above, they have provided sufficient guidance that an artisan of ordinary skill, such as a clinician, could obtain and/or prepare and administer the recited glycyrrhizin compounds without undue experimentation. Applicants therefore assert that claim 7 is therefore fully enabled by the specification. With respect to the Examiner's assertion that claim 7 lacks utility, Applicants suggest that there is at least a reasonable correlation between the demonstrated ability to inhibit MCP-1 and the asserted utility of the recited glycyrrhizin derivatives. Applicants note that there is no requirement to prove such a correlation as a

matter of statistical certainty, rather all that is required is a reasonable correlation between the activity and the asserted use.

Applicants note that in combination with such a reasonable correlation, that "data generated using in vitro assays, or from testing in an animal model or a combination thereof almost invariably will be sufficient to establish therapeutic or pharmacological utility for a compound, composition or process" (see MPEP § 2107.03).

Applicants have provided data that supports the asserted utility of claim 7, and suggest that the disclosure would be reasonably predictive of their asserted utility when considered by one skilled in the art. In view of the amendments and remarks above, Applicants request the withdrawal of the rejection of claim 7 under 35 U.S.C. § 112, first paragraph.

The Examiner has rejected claims 1-3, 5 and 6 under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter that Applicants regard as their invention. In particular, claim 5 is considered indefinite because it is not clear from claim 5 how the inhibition production of MCP-1 is achieved. Claims 1-3 and 6 are considered indefinite because the claims do not set forth any steps in the claimed method.

As Applicants have canceled claims 5 and 6, the rejection of those claims under 35 U.S.C. § 112, second paragraph, is rendered moot. With respect to claims 1-3, Applicants have amended claim 1 to recite the administration of a compound for inhibiting MCP-1 production. In view of the above amendments, Applicants request the withdrawal of the rejections of claims 1-3 under 35 U.S.C. § 112, second paragraph.

Rejections under 35 U.S.C. § 101

Claims 1-3 and 6 are rejected under 35 U.S.C. § 101 because the claimed recitation of a use, without setting forth any steps, results in an improper definition of a process.

As discussed above, claim 1 has been amended to recite the administration of a compound for inhibiting MCP-1 production. Applicants suggest that, as amended, claims 1-3 properly recite a process or method, and request the withdrawal of the rejection of claims 1-3 under 35 U.S.C. § 101.

Rejections under 35 USC § 102

Claims 1-7 are rejected under 35 U.S.C. § 102(b) as being anticipated by European Patent No. 0255 420, or in the alternative, claims 1-7 are rejected under 35 U.S.C. § 103(a) as being obvious over European Patent No. 0255 420 (hereafter Ito et al.). The Examiner indicates that Ito et al. discloses a composition comprising glycyrrhizin and a method administering said composition, and that the inhibition of MCP-1 production would have been inherent in such an administration.

Without acknowledging the propriety of the rejections, Applicants have amended claim 1 to recite a method of treating a mammal. Applicants suggest that the Ito et al. reference discloses glycyrrhizin only as an antiviral agent for inhibiting the growth of HIV, and does not disclose the treatment of entire organisms. Therefore Ito et al. fails to teach or suggest the use of glycyrrhizin for inhibiting MCP-1 production in a mammal, as

recited in claim 1, as amended. Applicants suggest that Ito et al. also fails to teach a pharmaceutical composition according to claim 7, and fails to teach or suggest the use of glycyrrhizin for treating or preventing decreases in infection resistance, as recited in new claim 9.

In order to anticipate a claim, or in order to establish *prima facie* obviousness under 35 U.S.C. § 103, each and every element of the claim must be found in the prior art. As Ito et al. fails to disclose each and every element of claims 1, 7, and 9, Applicants suggest those claims are not anticipated by Ito et al., and that claims 2, 3, 8, and 10-13, which depend directly or indirectly from claims 1 and 9, are similarly not anticipated by the Ito et al. reference. Applicants suggest that Ito et al. fails to establish the *prima facie* obviousness of claims 1-3, and 7-13.

Claims 1-7 are rejected under 35 U.S.C. § 102(b) as being anticipated by Takei et al. (Abstract T-14, ASM 101st General Meeting, 5/22/2001). The Examiner indicates that Takei discloses the claimed method of inhibiting MCP-1 with glycyrrhizin. Applicants disagree.

Applicants note that the disclosure of Takei et al. describes the inhibition of MCP-1 in peripheral blood mononuclear cells derived from AIDS patients. As Takei et al. fails to disclose the administration of the recited glycyrrhizin derivatives to a mammal, and as claim 1 recites the administration of a glycyrrhizin to a mammal, Takei et al. necessarily fails to anticipate the subject matter of claim 1.

Claim 7 recites a pharmaceutical composition for treating or preventing decreases in infection resistance in selected individuals. Takei et al. fails to disclose such pharmaceutical compositions. Therefore Takei et al. fails to anticipate the subject matter of claim 7.

Claim 9 recites a method of treating or preventing decreases in infection resistance that includes administration of a recited glycyrrhizin derivative. Takei et al. fails to disclose such a method of treating or preventing decreases in infection resistance. Therefore Takei et al. fails to anticipate the subject matter of claim 9.

As claims 2, 3, 8, and 10-13 depend directly or indirectly from claims 1, 7, and 9, claims 2, 3, 8, and 10-13 are not anticipated by Takei et al. for at least the same reasons as claims 1, 7, and 9. In view of the above amendments and remarks, Applicants respectfully request the withdrawal of the rejection of the claims1-3 and 7 under 35 U.S.C. § 102.

It is now believed that the subject patent application has been placed in condition for allowance, and such action is respectfully requested. If the Examiner has any questions or concerns, or if a telephone interview would in any way advance prosecution of the application, please contact the undersigned agent of record.

The Commissioner is hereby authorized to charge any additional fees which may be required, or credit any overpayment to Deposit Account No. 11-1540.

CERTIFICATE OF MAILING

I hereby certify that this correspondence is being deposited with the United States Postal Service as first class mail, postage prepaid, to: Mail Stop Amendment, Commissioner for Patents, P.O. Box 1450, Alexandria, Virginia 22313-1450 on January 17, 2005.

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